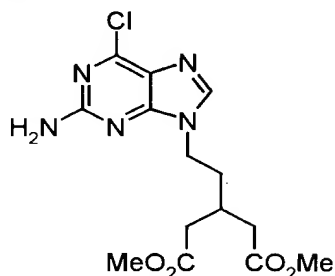


Rejection under 35 USC §102 (b)

Claim 5 is rejected under 35 USC §102(b) as being anticipated by EP 302,644. Applicants respectfully traverse this rejection.

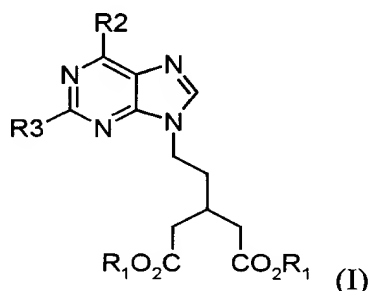
The compound of Claim 5 is



and is additionally shown in the Jones Declaration, Stage 1, Step I.

The EPO 302644 ('644) referred to by the Examiner as teaching this compound is incorrect. The Examiner refers to Formula (I) therein where "R₃ as amino is clearly preferred, as it is the sole choice seen in the final product. As for R₁, two choice are given as preferred at page 7, line 7, viz., methyl and ethyl", etc.

EPO 302 644 teaches Formula (I) to be a genus of compounds having the structure:



wherein

R₁ is C₁₋₆ alkyl, or phenyl C₁₋₆ alkyl in which the phenyl group is optionally substituted; R₂ is hydrogen, hydroxy, chlorine, C₁₋₆ alkoxy, phenyl C₁₋₆ alkoxy or amino; R₃ is halogen, C₁₋₆ alkylthio, C₁₋₆ alkylsulphonyl, azido, an amino group, or a protected amino group.

Using this genus of compounds taught by Formula (I), the compound of Claim 5 is not anticipated as the combination of substituents is far to large to achieve this particular species.

However, the Examiner points to page 7, line 7, which states "Values for R₁ in compounds of formula (I) include C1-4 alkyl, for example methyl and ethyl." The formula has two R₁ groups that for methyl and ethyl yield the following combinations:

methyl/methyl, methyl/ethyl and ethyl/ethyl. If you broaden this to the C₁₋₄ group as methyl and ethyl are only illustrative, the combination is much larger.

Page 7, line 8 and 9 teach "Values for R₂ in compounds of formula (I) include hydrogen, chlorine, and C₁₋₄ alkoxy, for example methoxy." As methoxy is only illustrative, use of C₁₋₄ alkoxy encompasses more than 8 possibilities, in addition to the first 2.

With respect to the statement by the Examiner that "R₃ as amino is clearly preferred, as it is the sole choice seen in the final product" is also incorrect in that just because an amino functionality is present in the final compound(s) does not mean that its presence would be preferred in a chemical intermediate used in the synthesis of those final compounds. Indeed the skilled person may well consider that the presence of an amino group which is readily amenable to chemical modification in a chemical intermediate as undesirable and, would for example, consider a protected amino group to be preferable. In fact, page 7, line 10 and 11 appear to indicate that suitable values for R₃ include protected amino groups.

This reduction in the number of variables for the R₁/R₂ and R₃ moieties does not significantly decrease the number of permutations present that the skilled artisan would readily determine that the compound of Claim 5 was clearly anticipated by the disclosure of the 302 644 publication.

In light of this reconsideration and withdrawal of the rejection to the claims under 35 USC §102(b) is respectfully requested.

Rejection under 35 USC § 103

Claims 5 to 7, and 10 to 14 are rejected by the Examiner under 35 USC §103(a) as being unpatentable over EP 302,644 ('644) Applicant respectfully traverses this rejection.

The comparative examples presented in the previously submitted Jones declaration directly addressed the objections raised by the Examiner in his action dated 14 June 1999 (page 6 points A-C). The Examiner alleged that the advantages obtained using the process of the invention may not be due to the presence of the chloro until after the decarboxylation step as claimed, but may be due to the different reagents, temperatures, etc. highlighted in points A-C.

The Jones declaration compares two routes to famciclovir which differ only in that one removes the Cl prior to decarboxylation as in EP 302644 and the other removes the Cl after decarboxylation as in the claimed invention. The results presented

show unambiguously that the advantages are due to the Cl substituent and not due to any other conditions. The Examiner now appears to comment that this declaration is insufficient because we used the same reaction conditions to compare the two examples.

A comparison using different conditions as set out in points A-I of the present action has already been done in that the process of EP 302644 gave a yield of 10.6% whereas the process of the invention gave a yield of 41% (see pages 5 and 6 of the description).

The process of the Jones declaration does fall within claim 10 as a decarboxylation, i.e. removal of $\text{-CO}_2\text{Et}$, does take place, the fact that the conditions chosen also results in a transesterification of the 2 remaining $\text{-CO}_2\text{Et}$ groups is irrelevant as claim 10 recites "... which process comprises ...".

The Examiners comments pointing out that the process of EP 302644 gave a crystalline product yet the process in our declaration gave a useless brown oil only further highlights the surprising advantages obtained using the process of the invention. In particular it supports the arguments previously presented that the process of the invention allows for the production of a pure product in high yield without the need for the chromatographic purification steps, which were necessary in EP 302644 (using the reaction conditions as we now claim, not as compared).

The present process was developed as an improvement to the bromotriester route of EP 302644 in order to facilitate large scale commercialization of the process.

The teachings of the EPO 302644 reference would not lead the skilled artisan to carry out the sequence of steps as presently claimed herein, i.e. coupling, decarboxylation, reduction and esterification, followed finally by removal of the 6-chloro substituent.

The unexpected results achieved by retention of the 6-chloro throughout the claimed process is significant and is has been confirmed by the Declaration of Dr. Jones.

These particularly advantageous and unexpected features of the present invention are not taught, nor are they suggested in the '644 application. The skilled artisan would not be motivated by the '644 reference to retain the chlorine in the chemical intermediates. A skilled artisan would not be directed to the improved benefits of yield in the decarboxylation step, nor to the improved yields in the reduction and acetylation steps.

•USSN 09/265,926
Art Unit: 1624

- 7 -

In light of these remarks and claim amendments, reconsideration and withdrawal of the rejection to the claims under 35 USC §103 is respectfully requested.

Conclusion

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. It is not believed that this paper should cause any additional fees or charges to be required, other than expressly provided for already. However, if this is not the case the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



Dara L. Dinner
Attorney for Applicant
Registration No. 33,680

SmithKline Beecham Corporation
Corp. Intellectual Property (UW2220)
P.O. Box 1539
King of Prussia, PA 19406-0939
(610) 270-5017 - telephone
(610) 270-5090 - facsimile
30920C1X1OA1.doc